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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,254	12/06/2000	Augusto Inventi Solari	P101615 -0000	8796

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EXAMINER
MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
1652	17

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,254	SOLARI ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10,11 and 18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,11 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

Applicant's Amendment C, Paper No. 16 filed July 7, 2003, amends claim 1, 4-8, 10, 11, 18 and 19, cancels claims 9 and 12-17, and adds the new claims 20 and 21, thus claims 1-8, 10, 11 and 18-21 are pending in the application. The amendments to the independent claims 1, 18 and 19 require that all claimed DNA molecules, plasmids, host cells, and processes of using host cells for bioconversions providing, or fermentations producing, doxorubicin, comprise, contain, or utilize a specific nucleic acid restriction fragment described at, e.g., lines 4 and 5 of the amended claim 1. This 2.3 kilobase *Xba*I-*Hin*dII restriction endonuclease digest fragment was prepared, see Figure 2a, page 3, lines 16-22, page 6, lines 2-5, page 8, lines 12-14, and page 12, lines 5-11, for insertion in Applicant's claimed plasmids pIS284 and pIS287, from a prior art plasmid, pWHM603, disclosed by Guilfoile and Hutchinson, 1991, made of record herewith. The intermediate plasmid that Applicant chose to use, pBluescriptII SK+, and its multiple cloning site [mcs] permitting extraction of an inserted nucleic acid segment by restriction with endonucleases different from the endonuclease(s) used for inserting a segment in the mcs, was designed for these manipulations and commercially available, as well as widely used for such manipulations, at the time the invention was made.

Because the record does not disclose that Applicant's plasmids pIS284 or pIS287, which both comprise the 2.3 kilobase *Xba*I-*Hin*dII restriction endonuclease fragment of claims 1, 18, and 19, will be made freely available to the public during the term of any patent issuing on the instant application, or that the or the prior art plasmid pWHM603 will be made freely available to the public during the term of any patent issuing on the instant application, and because the amended claims 7 and 20 describe the invention that is either of the plasmids pIS284 or pIS287, or the use of either, a new ground of rejection

and requirement for deposit of biological materials is made herein. Because the originally filed claim 13 had also described the invention that is either of the plasmids pIS284 or pIS287 and the requirement for the deposit of biological materials and accompanying rejection could have been made in either of Papers Nos. 11 or 14 mailed, respectively, June 27, 2002, and March 7, 2003, this communication is not made final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10, 11 and 18-21 are rejected under 35 U.S.C. §112, first paragraph, because the description of the specification is not enabling for the DNA region comprising both the *Streptomyces peucetius drr*A and *drr*B genes within a 2.3kb *Xba*I-*Hin*dII restriction endonuclease fragment, or enabling for the plasmids pIS284 or pIS287 which both comprise this DNA region. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and use the invention commensurate in scope with these claims.

This is a new ground of rejection. Claims 1, 7 and 18-20 all describe an invention having a specific, unique, biological material, thus present an issue of enablement because the specification does not disclose and enable, e.g., as a DNA sequence in the sequence disclosure, the nucleic acid sequence of the DNA region comprising both of the *S. peucetius drr*A and *drr*B genes within a 2.3kb *Xba*I-*Hin*dII restriction endonuclease fragment. This DNA region is comprised by the plasmids pIS284 and pIS287, consequently, the specification does not fully disclose and enable either plasmid. Claims 2-6, 8, 10, 11 and 21 are subject to this rejection in view of their dependency from claim 1. Neither does the specification disclose that the claimed biological materials are freely available to the public, either currently or upon the issuance of a patent wherein the claimed biological materials are essential to the subject matter. The present record provides no indication, e.g., of a deposit receipt of an issuing depository indicating that the

fee for maintenance of the deposits of biological material described by claims 1, 7 and 18-20 for 20-30 years has been charged to and paid by the assignee. If such a deposit has been made, or will be made, it is noted that deposits under the terms of the Budapest Treaty are, in themselves, insufficient to satisfy 37 CFR §§1.805-1.807 unless they are disclosed on the record to be freely available to the public should a U.S. patent issue on the instant application. See, *Ex parte Hildebrand*, 15 USPQ2d 1662, 1664 (1990) (restrictions must "be irrevocably removed upon the issuance of [a] patent" because a residual requirement of secrecy resides in Rule 9.2 of the Budapest Treaty). See also, MPEP §608.01(p)(C)(3). Where 37 CFR §1.801, et seq., is applied to a deposit, including a Budapest Treaty deposit, submission of a declaration or averment, either by the **assignee** or the **attorney of record** over his or her signature and registration number, that gives these two assurances provides a basis for an enabling disclosure:

1) that all restrictions on the availability to the public of the deposited material will be removed, and,
2) that the viability of the deposits will be maintained,

both for the duration of the patent term or for a period of twenty years in accordance with 37 CFR §§1.805-1.807. See, MPEP §§2405-2411.05, wherein the latter section requires an amendment to the specification that introduces specific information concerning any deposit of biological materials. Such an amendment does not constitute new matter.

In the alternative, Applicant may show that the artisan can reconstruct the nucleic acid sequence region critical to the claims, in its particulars, utilizing a nucleic acid sequence of the prior art plasmid pWHM606 not set forth by Guilfoile and Hutchinson in their journal publication, but otherwise available, with the removal of the sequence regions eliminated by the *Bgl*II restriction endonuclease and subsequent single-strand exonuclease digestions and the incorporation of those portions of the pBlusescriptII SK+ mcs nucleic acid sequence flanking its *Sma*I insertion site and extending to its *Xba*I and *Hind*III cleavage sites.

Allowable Subject Matter

While subject to the new ground of rejection set forth above, claims 1-8, 10, 11 and 18-21 are free of the prior art of record. One of ordinary skill in the art at the time the invention was made would have appreciated the benefits of including a DNA region encoding the *drr*A and *drr*B genes of *S. peucetius* in a plasmid designed for doxorubicin conversion, or for doxorubicin production, in a transformed host cell and would have been familiar with the use of multiple cloning sites in commercial maintenance and expression plasmids, such as pBlusescriptII SK+. Such an artisan would also have found Applicant's manipulations of the pBlusescriptII SK+ mcs and the coding region comprising the *drr*A and *drr*B genes in the plasmid pWHM606 of Guilfoile and Hutchinson routine. Yet the prior art of record fails to provide any specific motivation to select *Bgl*II sites flanking the *drr*A and *drr*B genes in the prior art plasmid pWHM606 for digestion to prepare successor plasmids, either for doxorubicin conversion or doxorubicin production because neither the publication of Guilfoile and Hutchinson, nor any other prior art of record, indicates that *Bgl*II sites are proximal to the *drr*A and *drr*B coding region. Instead, Figure 1 of Guilfoile and Hutchinson indicates that no *Bgl*II site is within 1 kb of the combined coding region, and does not disclose a flanking *Bgl*II site within 5 kb of the transcription origin of the combined coding region.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM-5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. Further fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. The examiner's direct FAX telephone number is 703.746.3169. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
July 31, 2003

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